METHOD FOR PRODUCING ONCOLYSIS

This application is a continuation of application Ser. No. 419,324 filed Sept. 17, 1982, now abandoned.

Reference is made to Disclosure Document No. 096829 filed by the present inventor on Jan. 9, 1981 which relates to the present invention. Permanent retention thereof is hereby requested.

BACKGROUND OF THE INVENTION

When the adenosine triphosphate (ATP) pool in a cell is depleted below the level which must be maintained to meet the cellular needs for maintenance of metabolic processes, the cell is not only incapable of mitotic division but the cell dies. The rate of change in the ATP pool size existing in a cell at any particular time is the difference between the rate at which ATP is being produced, primarily by oxidative phosphorylation along the respiratory chain (RC) in the mitochondria, and the rate at which ATP is being used up (hydrolyzed) to provide substantially all the energy requirements of the cell. This energy is principally required for all the myriad anabolic and catabolic reactions in the metabolism of the cell, and for powering the "sodium pumps" of the pericellular membrane—whose collective action keeps the intracellular Na^+-concentration relatively low despite the continuous leakage of Na^+ through the membrane into the cell from the high Na^+-concentration extracellular fluid. The fundamental pathway involved in ATP production and usage (hydrolysis) in all normal body cells is depicted in FIG. 1.

The abbreviations used in FIG. 1 and elsewhere throughout this application are explained in the following table:

TABLE

AA	amino acids
AcCoA	acetyl coenzyme A
ADP	adenosine diphosphate
Amr	active metabolic rate
ATP	adenosine triphosphate, the basic compound for storing chemical energy in the cell
ATPase	adenosine triphosphatase
Bmr	basal metabolic rate (expressed as a multiple of pretreatment Bmr or Mayo Normal Standard Bmr)
Ca	calcium
CAC	Citric Acid Cycle
Cho	carbohydrate component of Dnr
Cl^-	ion
d	day
DNP	2,4-dinitrophenol
Dnr	defined nutritional regimen
Efa	essential fatty acid component of Dnr
EMP	Embden-Meyerhof Pathway
Emr_A	effective (average) metabolic rate
FA	fatty acids
g	gram
I	iodine
Kcal	kilocalories
kg	kilogram
lO_2/d	liters of O_2 consumed metabolically, per day (24 hours)
Mg	magnesium
mg	milligram
ml	milliliter
Mn	manganese
Na^+	sodium ion
NADH	reduced nicotinamide adenine dinucleotide
O_2	molecular oxygen
O/P	oxidative phosphorylation
P	phosphorus
Pr	protein component of Dnr
Pr = 15	denotes protein allowance basis for Dnr-protein; 15 g protein per 70 kg body weight
Pr_{min}	minimum protein allowance to maintain nitrogen equilibrium
RC	respiratory chain
Se	selenium
SP	sodium pump
UA	uncoupling agent
V + M	vitamins + minerals mix (daily amount supplied)
W_B	body weight (kg)
Zn	zinc

In normal (i.e., nonmalignant) body cells, the key nutritional component from which the fundamental energy supply for synthesizing ATP is derived is glucose. Glucose is transformed by the sequential reactions of the Glycolytic or Embden-Meyerhof Pathway (EMP) into pyruvate. Subsequently, pyruvate is decarboxylated and forms acetyl coenzyme A (AcCoA) which then enters the citric acid cycle (CAC) in the mitochondria. Here each acetate moiety, after first being incorporated into a molecule of citric acid, is broken down into CO_2 and H with the H appearing, inter alia, in molecules of reduced nicotinamide adenine dinucleotide (NADH) which then contain a large fraction of the energy contained in the original glucose. This NADH subsequently is oxidized in the mitochondrial respiratory chain (RC) with the ultimate production of H_2O by terminal reaction of the H with molecular O_2; this O_2 is readily supplied by the normal vasculature. The energy obtained by the transport of electrons down the potential gradient of the RC, by a sequence of redox reactions, is used to produce the ATP of the cell. Thus, in normal cells, the ATP-stored energy is obtained in the major proportion from nutritional glucose or from carbohydrates (i.e., starches and sugars) yielding glucose upon digestion. Some ATP-energy is obtained in normal cells from the oxidation, in the citric acid cycle, of fatty acids and amino acids obtained from nutritional fats and proteins. When adequate glucose is available in the nutriment intake, however, all major ATP-energy needs of normal cells are readily obtainable from glucose alone. The ATP produced in the respiratory chain enters the cellular "ATP Pool", from which it is continuously withdrawn to supply the energy needs of total cellular metabolism and to power the membrane sodium pumps which keep the intracellular Na^+-concentration adequately low by the outpumping of Na^+.

This same general pattern of ATP generation and usage obtains in malignant cells, but with two crucial differences. First, it has been extensively demonstrated that malignant cells in general possess a distinctive metabolic aberrancy, ostensibly as an innate consequence of their transformation to the malignant state. Under in vivo conditions, malignant cells in tumors do not substantially convert pyruvate to AcCoA (see FIG. 2); the pyruvate instead is essentially converted to lactate and is excreted from the cell. [Busch, H., *An Introduction to the Biochemistry of the Cancer Cell* Chapter 10, Academic Press, New York (1962)]. The net consequence is that only a very small fraction of the chemical energy in glucose can be extracted and used by the cancer cell, compared to that available to the normal cell. Since nutritional glucose is by far the most prominent and important source of normal cellular ATP energy under normal conditions, this transformation aberrancy puts the malignant cell at a great disadvantage regarding the